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10/511,813	10/19/2004	Johannes Coy	4007.008	6538

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EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,813	COY, JOHANNES	
	Examiner	Art Unit	
	Sean E. Aeder	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-39 and 41-64* is/are pending in the application.

4a) Of the above claim(s) *39,41-43 and 51-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-38 and 44-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Amendments and Remarks filed 9/13/07 in response to the Office Action of 6/13/07 are acknowledged and have been entered.

Claims 34-39 and 41-64 are pending.

Claims 39, 41-43, and 51-64 have been withdrawn.

Claims 34, 44, 49, and 50 have been amended by Applicant.

Claims 34-38 and 44-50 are currently under examination.

Rejections Withdrawn

The rejection under 35 U.S.C. 102(e) is withdrawn in view of amendments.

The rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of amendments.

The rejection under 35 U.S.C. 112 first paragraph, for recitation of new matter, is withdrawn in view of amendments.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-38 and 44-50 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for the reasons stated in the Office Action of 6/13/07 and for the reasons set-forth below.

The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the amended claims are inclusive of a genus of transketolase like-1 genes whose complement hybridizes under stringent conditions to SEQ ID NO:1. However, the written description in this case only sets forth human transketolase like-1 genes comprising the sequence set-forth in SEQ ID NO:1. The specification does not disclose, and the prior art does not teach, the genus of transketolase like-1 genes whose complement hybridizes under stringent conditions to SEQ ID NO:1. Due to the ability of polynucleotide sequences sharing a relatively low degree of homology to hybridize under stringent conditions, it is noted that there is a large variation between SEQ ID NO:1 and the genus of transketolase like-1 genes whose complement hybridizes under stringent conditions to SEQ ID NO:1.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common to that genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by

nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Further, in regards to claims to a product defined by function (the ability to hybridize to SEQ ID NO:1), without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. See Eli Lilly, 119 at1568 USPQ2d at 1406 ("definition by function...does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is").

The inventions at issue in Lilly were DNA constructs per se, the holdings of that case is also applicable to claims such as those at issue here. Further, disclosure that does not adequately describe a product itself logically cannot adequately describe a method of detecting that product.

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., F.3d, 2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of transketolase like-1 genes that encompass the genus nor does it provide a description of structural features that are common to the genus. Further, this genus encompasses variants. In regards to genera encompassing variants, Applicant is directed to Example 13 of the Synopsis of Application of Written Description Guidelines

(http://www.uspto.gov/web/menu/written.pdf), which addresses claims drawn to a genus of polypeptide variants. Example 13 states that even when a specification discloses that changes which produce variants are routinely done in the art, the specification and the claims do not provide any guidance as to precisely what changes should be made. Structural features that could distinguish the compounds of the claimed genus from others not encompassed by the genus are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is needed. Since the disclosure fails to describe common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of SEQ ID NO:1 is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description

requires more than a mere statement that it is part of the invention and reference to a potential method of isolation. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

In the Reply of 9/13/07, Applicant amended claims 34 and 44 to remove references to 80% homology.

The amendments to the claims have been carefully considered, but are not deemed persuasive. While the pending claims are no longer drawn to detecting a genus of transketolase like-1 genes whose complement hybridizes under stringent conditions to "a sequence having at least 80% homology to" SEQ ID NO:1, the pending claims are drawn to detecting the broad genus of transketolase like-1 genes whose complement hybridizes under stringent conditions to SEQ ID NO:1. For the reasons discussed above, and because of the *great* variation in sequences whose complement would hybridize under stringent conditions to SEQ ID NO:1, the specification fails to comply with the written description requirement.

Claims 34-38 and 44-50 remain rejected under 35 U.S.C. 112 first paragraph, for failing to comply with the enablement requirement, for the reasons stated in the Office Action of 6/13/07 and for the reasons set-forth below.

While being enabling for an in vitro method for detecting colon cancer in an individual comprising detecting in a biological sample comprising colon cancer cells obtained from said individual the level of polynucleotides comprising SEQ ID NO:1 and comparing said level to the level of polynucleotides comprising SEQ ID NO:1 in a control sample comprising normal colon cells, wherein a higher level of polynucleotides comprising SEQ ID NO:1 in said biological sample as compared to said control sample indicates that said individual has colon cancer, does not reasonably provide enablement for an in vitro method for detecting every type of disorder characterized by abnormal cell proliferation in an individual comprising detecting in just any biological sample obtained from said individual and just any normal control sample a level of expression of just any transketolase like-1 gene whose complement hybridizes under stringent conditions to SEQ ID NO:1, wherein a higher level of expression in the biological test sample as compared to the level of expression in the normal control samples indicates that said individual has at least one of any disorder characterized by abnormal cell proliferation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They

include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The instant claims are broadly drawn to an in vitro method for detecting every type of disorder characterized by abnormal cell proliferation in an individual comprising detecting in any biological sample obtained from said individual and any normal control sample a level of expression of any transketolase like-1 gene whose complement hybridizes under stringent conditions to SEQ ID NO:1, wherein a higher level of expression in the biological test sample as compared to the level of expression in the normal control samples indicates that said individual has at least one of any disorder characterized by abnormal cell proliferation. It is noted that genes whose complements hybridize under stringent conditions to SEQ ID NO:1 would include many genes unrelated to the transketolase like-1 gene of SEQ ID NO:1 that would not predictably exhibit the same expression pattern as SEQ ID NO:1.

The specification teaches an in vitro method for detecting colon cancer in an individual comprising detecting in a biological sample comprising colon cancer cells obtained from said individual the level of polynucleotides comprising SEQ ID NO:1 and comparing said level to the level of polynucleotides comprising SEQ ID NO:1 in a control sample comprising normal colon cells, wherein a higher level of polynucleotides comprising SEQ ID NO:1 in said biological sample as compared to said control sample

indicates that said individual has colon cancer (Figure 1, in particular). Further, the specification clearly discloses that "transketolase like-1 gene" polynucleotides include variants of SEQ ID NO:1 (page 7) and makes a clear distinction between said variants and "the human translocases like-1 gene as given in SEQ I D NO:1" that is disclosed to be overexpressed in certain cancerous tissues as compared to corresponding normal controls (see lines 7-12 of page 3, in particular).

The state of the prior art dictates that if a molecule such as a polynucleotide comprising SEQ ID NO:1 is to be used as a surrogate for a diseased state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the polynucleotide to be used in a diagnostic manner. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful application. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome.

The level of unpredictability for the detection of any disease is quite high. Since neither the specification nor the prior art provide evidence of a universal association between the claimed method and every type of disorder characterized by abnormal cell proliferation, every type of sample, and expression of just any gene whose complement hybridizes to SEQ ID NO:1, a practitioner wishing to practice the claimed invention would be required to provide extensive experimentation to demonstrate such an association. Such experimentation would in itself be inventive.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to an in vitro method for detecting every type of disorder characterized by abnormal cell proliferation in an individual comprising detecting in any biological sample obtained from said individual and any normal control sample a level of expression of any transketolase like-1 gene whose complement hybridizes under stringent conditions to SEQ ID NO:1, wherein a higher level of expression in the biological test sample as compared to the level of expression in the normal control samples indicates that said individual has at least one of any disorder characterized by abnormal cell proliferation, and Applicant has not enabled said method because it has not been shown that diagnosis of every disorder characterized by abnormal cell proliferation is predictably indicated when the level of expression of any transketolase like-1 gene whose complement hybridizes to SEQ ID NO:1 in just any biological sample is greater than the level of expression in just any control sample.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of

skill in the art to determine with any predictability, that the method would function as claimed.

In the Reply of 9/13/07, Applicant states that the instant specification describes translocase like-1 gene (TLK1) as being overexpressed in colorectal cancer (lines 8-10 of page 9), colon carcinoma (lines 27-28 of page 37), lung adenocarcinomas (lines 27-28 of page 37), and carcinomas of the stomach (lines 27-29 of page 37). Applicant further states that the specification states that staining of TKTL1 could be observed in breast, lung, cervical, gastric, oesophageal, endometrial, and ovarian carcinomas (lines 4-7 of page 39). Applicant further provided several references that teach overexpression of TKTL1 in various samples of various cancers and the use of inhibitors of TKTL1 with various cancers. Based on these references, Applicant concludes that TKTL1 overexpression is indicative of the presence of disorders characterized by abnormal cell proliferation, including but not limited to colon cancer.

The amendments to the claims and the arguments found in the Reply of 9/13/07 have been carefully considered, but are not deemed persuasive. In regards to the statement that (TLK1) is overexpressed in colorectal cancer, colon carcinoma, lung adenocarcinomas, and carcinomas of the stomach, *the instant claims are not drawn to detecting expression of a specific TLK1*. Rather, the instant claims are broadly drawn to detecting expression of any gene whose complement hybridizes under stringent conditions to SEQ ID NO:1. As evidenced by the newly submitted teachings of Langbein et al (British Journal of Cancer, 2006, 1-8) TKT, TLK1, and TLK2 are highly similar translocases encoded by separate genes (see left column of page 3, in

particular). Due to their high similarity to TLK1, genes whose complements hybridize under stringent conditions to SEQ ID NO:1 would include TKT and TLK2. As further evidenced by Langbein et al, TKTL2 is underexpressed in colon carcinoma tissue as compared corresponding normal colon tissue (see Table 1, in particular) and overexpression of TKT was not detected in any of 54 carcinoma tissues tested (see left column of page 3, in particular). Therefore, the Reply of 9/13/07 provides clear evidence that the instant claims could not be practiced as broadly claimed with any predictability of success. Further, arguments directed at determining overexpression of a specific TKTL1 are not in commensurate with the scope of the claims, as the claims are broadly drawn to detecting all genes whose complements hybridize under stringent conditions to SEQ ID NO:1.

In regards to the statement that the specification states that staining of a specific TKTL1 could be observed in breast, lung, cervical, gastric, oesophageal, endometrial, and ovarian carcinomas, the specification does not disclose results of differential staining of just any gene whose complement hybridizes under stringent conditions to SEQ ID NO:1 in breast, lung, cervical, gastric, oesophageal, endometrial, and ovarian carcinomas as compared to corresponding normal controls. Further, from the teachings of Tockman et al, one of skill in the art would recognize that mere expression of a molecule in tissue of a particular carcinoma does not indicate that said molecule would predictably function as a marker for said carcinoma by assaying expression of said molecule in just any biological test sample and just any control. There must be some expression pattern that would allow the molecule to be used in a diagnostic manner.

In regards to the submitted references that teach overexpression of a specific TKTL1 in various samples of various cancers and the use of inhibitors of TKTL1 with various cancers, *the instant claims are not drawn to detecting expression of TLK1*. Rather, the instant claims are broadly drawn to detecting expression of any gene whose complement hybridizes under stringent conditions to SEQ ID NO:1. Further,as evidenced by the newly submitted teachings of Langbein et al (British Journal of Cancer, 2006, 1-8) TKT, TLK1, and TLK2 are highly similar translocases encoded by separate genes (see left column of page 3, in particular). Due to their high similarity to TLK1, genes whose complements hybridize to SEQ ID NO:1 would include TKT and TLK2. As further evidenced by Langbein et al, TKTL2 is underexpressed in colon carcinoma tissue as compared corresponding normal colon tissue (see Table 1, in particular). Therefore, the Reply of 9/13/07 provides clear evidence that the instant claims could not be practiced as broadly claimed with any predictability of success.

Summary

No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a). A shortened statutory period for response to this Final Action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this Final Action and the

advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. '1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than six months from the date of this Final Action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA

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